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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/814,194	04/01/2004	Johan Frostegard	EPCL:011US	6446

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EXAMINER	
COOK, LISA V	
ART UNIT	**PAPER NUMBER**
1641	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/814,194	FROSTEGARD, JOHAN	
	Examiner	Art Unit	
	Lisa V. Cook	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8 and 11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/720,967.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. Applicant's response to the Office Action mailed June 20, 2006 is acknowledged (paper filed 12/18/06). In the amendments filed therein claims 1-8 were was modified. Claims 9-10 and 12-23 have been canceled. Currently claims 1-8 and 11 are pending and under consideration.

2. Objections and/or rejections of record not reiterated below have been withdrawn.

NEW GROUNDS OF REJECTIONS

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

I. Claims 1-2, 5-8 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Muzya et al. (Immunologiya, 1997, Vol.6, pages 9-11, Collective of Authors, 1997 UDC 618.3-092:812.087.1]-078-33, submitted by applicant on 12/5/06) in view of Roudebush et al. (Journal of Assisted Reproduction and Genetics, Vol.11, No.8, 1994).

Muzya et al. teach that antibodies involving that bind to PAF, lyso-PAF, and acyl analogs of PAF.

The binding of antiphosphatidylcholine antibodies to PAF and its structural analogs is related to the presence of phosphocholine fragments. The binding of antiphosphatidylcholine antibodies to PAF was exemplified in the sera of women with obstetrical-gynecological disorders (reading on spontaneous abortions). See abstract.

In particular, Muzya et al. teach an enzyme immunoassay (EIA) to study the binding of antibodies that bind to PAF and its structural analogues. In the assay PAF (a type of phosphocholine as exemplified in the specification on page 14 lines 12-11) was placed on polystyrene microplates. The assay procedure also includes a reagent for detecting the antibodies bound to PAF (conjugates of murine monoclonal antibody with horseradish peroxidase IgM and IgG). See page 11, 2nd paragraph. The reagents are employed to measure PAF – antibody binding in blood serum test samples. The serum from a patient with late toxicosis in pregnancy had a high level of IgG antibodies that were reactive with PAF. The patient's serum bound significantly less to a PAF analogues. The researches taught that this may be caused by specific antibodies to PAF.

Although Muzya et al. teach the reagents required by the claims; they do not specifically teach the diagnosis of risk of spontaneous abortion.

However, Roudebush et al. teach the involvement of anti-platelet activation factor (PAF) antibodies in mouse pre-implantation embryo development. Mouse embryos cultured with anti-PAF significantly decreased embryo development compared to controls. Embryos cultured in anti-mouse IgG had no effect. The results, provide additional evidence that PAF is produced and secreted by cleavage-stage embryos and is required during the pre-implantation period. See abstract.

PAF is taught to play a significant role in reproduction, including but not limited to ovulation, fertilization, embryo development, and parturition. PAF production by pre-implantation embryos has been related to their subsequent implantation potential (Applicant's risk of spontaneous abortion). See page 414-Introduction. Anti-PAF antibodies significantly decreased hatched blastocyst development and the blocking of PAF with its specific antibody may abrogate events mediated by PAF. See page 416, 1st column.

It would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to take the anti-PAF detection assay methods as taught by Muzya et al. and employ them to evaluate obstetrical-gynecological disorders such as spontaneous abortions as taught by Roudebush et al. because Roudebush et al. taught that PAF play a significant role in reproduction, including but not limited to ovulation, fertilization, embryo development, and parturition. PAF production by pre-implantation embryos has been related to their subsequent implantation potential (Applicant's risk of spontaneous abortion). See page 414-Introduction. Anti-PAF antibodies significantly decreased hatched blastocyst development and the blocking of PAF with its specific antibody may abrogate events mediated by PAF. See page 416, 1st column.

Accordingly one having ordinary skill in the art would have been motivated to employ the measurement of antibodies to PAF to evaluate obstetrical-gynecological disorders or spontaneous abortions in order to detect/prevent/assess potential effects of said disorder.

II. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Muzya et al. (Immunologiya, 1997, Vol.6, pages 9-11, Collective of Authors, 1997 UDC 618.3-092:812.087.1]-078-33, submitted by applicant on 12/5/06) in view of Roudebush et al. (Journal of Assisted Reproduction and Genetics, Vol.11, No.8, 1994) and further in view of Barquinero et al. (Lupus, 1994, 3, 55-58).

Please see Muzya et al. in view of Roudebush et al.

Muzya et al. in view of Roudebush et al. differ from the instant invention in not specifically teaching assay measurements by enzyme-linked immunoassay.

However, Barquinero et al. teach an ELISA assay to measure antibodies against platelet-activating factor (PAF) in patients with autoimmune diseases. Specifically blood sample from patients with SLE (systemic lupus crythematosus), PAPS (antiphospholip syndrome), and syphilis. PAF was shown to be significantly present in patients with syphilis. See abstract and page 55 Introduction and page 56 "ELISA technique for anti-PAF".

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the reagents taught by Muzya et al. (Immunologiya, 1997, Vol.6, pages 9-11) in view of Roudebush et al. in an enzyme linked immunoassay (ELISA) as taught by Barquinero et al. (Lupus, 1994, 3, 55-58) because Barquinero et al. taught that the PAF ELISA could be used to detect syphilis. See Barquinero et al. abstract and page 55 Introduction and page 56 "ELISA technique for anti-PAF".

III. Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Muzya et al. (Immunologiya, 1997, Vol.6, pages 9-11, Collective of Authors, 1997 UDC 618.3-092:812.087.1]-078-33, submitted by applicant on 12/5/06) in view of Roudebush et al. (Journal of Assisted Reproduction and Genetics, Vol.11, No.8, 1994) and further in view of Smal et al. (Journal of Immunological Methods, Vol.128, 1990, pages 183-188).

Please see Muzya et al. in view of Roudebush et al.

Muzya et al. in view of Roudebush et al. differ from the instant invention in not specifically teaching assay measurements by radioimmunoassay.

However, Smal et al. teaches method to evaluate PAF in a specific and sensitive radioimmunoassay. In the procedure the anti-PAF antibodies showed specificity for the acetyl group at the C2 position of the PAF molecule and exhibited no significant cross-reactivity with lyso-PAF or the naturally occurring lipids. The RIA was at least as good as the platelet-based assay for PAF but the RIA was simpler to perform, had higher capacity and did not have the draw backs of the inherent variability associated with the bioassay. See abstract and pages 186-187.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to take the reagents taught by Muzya et al. in view of Roudebush et al. to measure PAF by radioimmunoassay procedures as exemplified by Smal et al. because Smal et al. taught that the RIA was at least as good as the platelet-based assay for PAF but the RIA was simpler to perform, had higher capacity and did not have the draw backs of the inherent variability associated with the bioassay. See abstract and pages 186-187.

Response to Arguments

4. Applicants arguments against the rejections of record are MOOT in light of the newly submitted claims. The rejections of record have been modified appropriately herein.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

The Declaration under 37 CFR 1.132 filed 12/18/06 by Dr. Frostegard is insufficient to overcome the rejection of claims 1-8 and 11 based upon Muzya et al. (Immunologiya, 1997, Vol.6, pages 9-11, Collective of Authors, 1997 UDC 618.3-092:812.087.1]-078-33, submitted by applicant on 12/5/06) as set forth in the last/instant Office action because: Dr. Fostegard contends that Muzya et al. limited their study to blood sera containing phosphatidylcholine antibodies by pre-selecting the blood samples for measurement. This argument was carefully considered but not found persuasive because the instant claims are drawn to a method employing the open language "comprising" and therefore reads on method having additional steps. Although the claims do not recite a pre-selection step of blood samples for analysis and merely "contact *any body fluid* capable of binding anti-PAF", the reference to Muzya et al. is still applicable.

Dr. Frostegard also contends that Muzya et al. makes no suggestion that antibodies to PAF can be used as a diagnostic tool for gynecological disorders.

This argument was carefully considered but not found persuasive because Muzya et al. teach that the serum from a patient with late toxicosis in pregnancy had a high level of IgG antibodies that were reactive with PAF. The patient's serum bound significantly less to a PAF analogues. The researches taught that this maybe caused by specific antibodies to PAF. Further Muzya et al. have been combined with Roudebush et al. Specifically, Roudebush et al. taught that PAF play a significant role in reproduction, including but not limited to ovulation, fertilization, embryo development, and parturition. PAF production by pre-implantation embryos has been related to their subsequent implantation potential (Applicant's risk of spontaneous abortion). See page 414-Introduction. Anti-PAF antibodies significantly decreased hatched blastocyst development and the blocking of PAF with its specific antibody may abrogate events mediated by PAF. See page 416, 1st column.

Applicant's arguments against the reference of Baldo et al. are MOOT because the reference has been removed/withdrawn.

5. For reasons aforementioned, no claims are allowed.

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

7. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 – Central Fax number is (571) 273-8300, which is able to receive transmissions 24 hours/day, 7 days/week. In the event Applicant would like to fax an unofficial communication, the Examiner should be contacted for the appropriate Right Fax number.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday - Friday from 7:00 AM - 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (571) 272-0823.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see httpr//pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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